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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/622,522	12/13/2000	Seishi Kato	GIN-6714CPUS	7220

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EXAMINER
WEGERT, SANDRA L

ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 04/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/622,522	KATO ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-15* is/are pending in the application.

4a) Of the above claim(s) *13-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicants' election without traverse of Group I, claim 1, in Paper 8 is acknowledged. In a second restriction, applicants also elected: SEQ ID NO: 4. Claims 1-6 were cancelled. Claims 7-15 were added by Amendment A (Paper 8, 2/12/02).

Newly submitted claims 13-15 are directed to an invention that is independent or distinct from the invention originally elected for the following reasons: Claims 13-15 recite SEQ ID NO's different from elected SEQ ID NO: 4. However each product represented by a SEQ ID NO is a distinct product having characteristic differences in structure and function and different uses as noted in Paper 6 (9/4/01). In addition, the search of several SEQ ID NO's would present an undue burden for the examiner.

Since applicant has received a Restriction/Election action and has elected the polypeptide of SEQ ID NO: 4, it is *this* invention that has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 13-15 are withdrawn from consideration as being directed to non-elected inventions. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 7-12 are under examination in the instant application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

Title:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "HUMAN RECEPTOR POLYPEPTIDE".

Appropriate correction is required.

Filing History

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 371 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78); this includes the PCT Application listed in the Declaration: PCT/JP99/00875 and Japanese patent application: 10/46607.

Appropriate correction is required.

Sequence Rules

The instant application is not fully in compliance with the sequence rules, 37 CFR 1.821-1.825, because each disclosure of a sequence embraced by the definitions set forth in the rules is

not accompanied by the required reference to the relevant sequence identifier (i.e., SEQ ID NO:). This occurs in Figures 1-7, for example. Sequence identifiers for Figures may be inserted into the figures themselves, or into the Brief description of the Figures.

Appropriate correction is required.

Abstract

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections/Objections

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of 35 U.S.C. 101:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7-12 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to the polypeptide of SEQ ID NO: 4, a peptide of 144 amino acids that the Applicant asserts contains motifs linking it to a transmembrane receptor (p. 1, second paragraph, for example). However, the specification does not disclose a function for the polypeptide of SEQ ID NO: 4 in the context of the cell or organism.

No well-established utility exists for newly isolated complex biological molecules. However, the specification asserts or implies the following as credible, specific and substantial patentable utilities for the polynucleotide encoding SEQ ID NO: 4 or the claimed polypeptide of SEQ ID NO: 4:

1) To make hybridization probes and primers,

2) To produce a variant nucleotide and polypeptide,

3) To localize gene expression in tissue samples,

4) To find drugs for the treatment or prevention of polypeptide deficiency,

5) For the production of antibodies.

Each of these will be addressed in turn:

1) To make hybridization probes and primers. This asserted utility is credible but not substantial or specific. Hybridization probes and primers can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

2) To produce a variant nucleotide and polypeptide. This asserted utility is credible but not substantial or specific. Such assays can be performed with any polynucleotide. Further, the specification discloses nothing specific or substantial for the variant nucleotide and polypeptide that is produced by this method. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

3) To localize gene expression in tissue samples. This asserted utility is credible but not substantial or specific. In situ hybridization probes can be designed from any polynucleotide sequence. Further, the specification does not disclose specific cDNA, DNA, or RNA targets. Since this asserted utility is also not present in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) To find drugs for the treatment or prevention of polypeptide deficiency. This asserted utility is credible and specific, however, it is not substantial. The specification does not disclose any conditions wherein there is a deficiency of the claimed polypeptide. Significant further experimentation would be required of the skilled artisan to identify individuals who would benefit from such a drug, and then to determine a best course of treatment. There is no disclosure, for example, of dosages or of how to assay for improvement or intolerable levels of side effects, etc. Since this asserted utility is not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

5) *For the production of antibodies.* This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the peptide or the nucleotides encoding the polypeptide of SEQ ID NO: 4, neither the polynucleotides, SEQ ID NO: 4, nor its antibodies have patentable utility.

Claims 7-12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 7-12 are directed to a polypeptide comprising the amino acid sequence of SEQ ID NO: 4.

The specification teaches the polypeptide of SEQ ID NO: 4. The disclosure also presents hydrophobicity data for the claimed polypeptide. However, the specification does not teach functional or structural characteristics of the polypeptide recited in the claims.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research 10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur

because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. Finally, Bork et al. (1996, Trends in Genetics 12:425-427) add that the software robots that assign functions to new proteins often assign a function to a whole new protein based on structural similarity of a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

Therefore, based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polypeptides to make a biologically active transmembrane protein without resorting to undue experimentation to determine what the specific biological activities of the polypeptide are.

The specification does not teach the skilled artisan how to use the claimed polypeptide for *any* purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the polypeptide such that the claimed polypeptides could be used as a diagnostic tool. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polypeptides for any purpose.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed polypeptides and fragments and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity and the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Furthermore, the specification does not reasonably provide enablement for *all variants* of SEQ ID NO: 4, as recited in claims 9-12. The disclosure does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The specification discloses the peptide of SEQ ID NO: 4. The specification asserts that the polypeptide is a transmembrane receptor peptide. Claims 9-12 recite contiguous fragments of SEQ ID NO: 4, ranging in length from 20 to approximately 72 amino acid residues. However, specific activities of these protein fragments, and assays to test for their activity, are not disclosed. There is no discussion, or working examples disclosed in the instant case, as to what amino acids are necessary to maintain the functional characteristics of the claimed polypeptides. The instant case claims altering as much as 75% of the claimed polypeptide of SEQ ID NO: 4. However, as discussed above, the art shows that receptor families have members

with *high* structural similarities but disparate functions. Bork et al. (1996, Trends in Genetics 12:425-427), as discussed above, shows that inaccurate statements of function attributed to new proteins is often based on structural similarity of a small domain of the new protein to a small domain of a known protein. As discussed above, it is seldom predictable as to which amino acids are necessary to maintain the functional characteristics of a new protein.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Due to the large quantity of experimentation required to determine how to use the polypeptide of SEQ ID NO: 4, the lack of direction or guidance in the specification regarding same (e.g., the lack of guidance regarding any specific activity of SEQ ID NO: 4), the lack of working examples to variants of SEQ ID NO: 4, the state of the art showing the unpredictability of function based on structural similarity of homologous proteins, and the breadth of the claims which embrace innumerable variants of SEQ ID NO: 4, undue experimentation would be required of the skilled artisan to make and use the claimed invention in its full scope.

Conclusion: Claims 7-12 are not allowable for the reasons cited above.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (703) 308-9346. The examiner can normally be reached Monday - Friday from 9:30 AM to 5:00 PM (Eastern Time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SLW
4/12/02

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER